



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2021-D-1152]

Considerations for Rescinding Breakthrough Therapy Designation; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Considerations for Rescinding Breakthrough Therapy Designation.” This guidance explains how, during its evaluation of a drug development program, FDA may consider whether to rescind a breakthrough therapy designation (BTD) that has been granted. The guidance is consistent with, and supplements, the information on BTD contained in the guidance for industry entitled “Expedited Programs for Serious Conditions--Drugs and Biologics” (May 2014) and in other BTD policies and procedures of the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) to expedite the development and review of a breakthrough therapy.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to

<https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2021-D-1152 for "Considerations for Rescinding Breakthrough Therapy Designation." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper

submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:

<https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002, or the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in

processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Dat Doan, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 3334, Silver Spring, MD 20993, 240-402-8926, Dat.Doan@fda.hhs.gov; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Considerations for Rescinding Breakthrough Therapy Designation.” This guidance is consistent with, and supplements, the information on BTM contained in the guidance for industry entitled “Expedited Programs for Serious Conditions--Drugs and Biologics” (May 2014)¹, in CDER’s Manual of Policies and Procedures 6025.6 “Good Review Practice: Management of Breakthrough Therapy-Designated Drugs and Biologics,” and in CBER’s Standard Operating Policy and Procedure 8212 Version 2 “Management of Breakthrough Therapy-Designated Products: Sponsor Interactions and Status Assessment Including Rescinding.”

Section 506(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 356(a)) provides for the granting of BTM “if the drug is intended, alone or in combination with 1 or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.” The BTM program is intended to facilitate and expedite the development of those drugs that receive designation and involves a resource commitment

¹ Available at: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/expedited-programs-serious-conditions-drugs-and-biologics>.

from FDA to provide early and frequent advice, conduct multidisciplinary meetings involving senior managers, and expedite the review of resultant marketing applications. Thus, over the course of product development, it is important that available evidence relevant to an application continues to meet the standards for BTB.

The information and circumstances supporting the original grant of BTB for a particular application may change over time. For example, if a different drug is approved to treat the unmet need that informed the rationale for granting BTB, the designated drug's preliminary clinical evidence may no longer meet the BTB criteria regarding substantial improvement over existing therapies (including the newly approved drug). In other cases, some drugs that appear promising in early development fail to meet their primary endpoints or the extent of benefit is more modest in later trials, and the magnitude of a treatment effect suggested by early development may not be replicable in later stages of development. Accordingly, in keeping with the Agency's authority to grant BTB only to drugs that meet the legal criteria, FDA periodically assesses whether the criteria for BTB continue to be met for designated products. If the designation is no longer supported by subsequent data, FDA may rescind the designation.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on "Considerations for Rescinding Breakthrough Therapy Designation." It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to

review by OMB under the PRA. The collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014; the collections of information in 21 CFR part 314 have been approved under OMB control number 0910-0001; the collections of information in 21 CFR part 601 have been approved under OMB control number 0910-0338; and the collections of information in section 506 of the FD&C Act have been approved under OMB control number 0910-0765.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs>, <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances>, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>, or <https://www.regulations.gov>.

Dated: June 17, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.